

### **REMARKS**

Applicant respectfully requests reconsideration. Claims 1-20, 22, 27-32, 43, 45-57, 63-65, 70-73, 76-80, 83, 84, 88, 89, 94, 95, 97 and 98 were previously pending in this application with claims 10-15, 29, 32, 45-57, 63-65, 70-73, 76-80, 83, 84, 88, 89, 94, 95, 97 and 98 withdrawn. By this amendment, no claims are cancelled or amended. As a result, claims 1-9, 16-20, 22, 27, 28, 30, 31 and 43 are pending for examination with claim 1 being an independent claim. No new matter has been added.

#### *Information Disclosure Statement*

Applicant thanks the Examiner for considering the Information Disclosure Statement filed December 5, 2006.

#### *Withdrawn Objections/Rejections*

The objections to the specification have been withdrawn. The rejection of claims 1-9, 16-20, 22, 17-28, 30, 31 and 43 under 35 U.S.C. § 112, second paragraph has been withdrawn.

#### Rejections Under 35 U.S.C. § 103

The rejection of claims 1-9, 16-20, 22, 27, 28, 30, 31 and 43 under 35 U.S.C. § 103(a) as being unpatentable over International Published Application No. WO 2001/22972 (Krieg et al.) has been maintained.

The Examiner's argument is that one of ordinary skill in the art would select and modify SEQ ID NO:888 from Krieg et al. to arrive at the instantly claimed SEQ ID NO:1, based on the modification in Krieg et al. of an unrelated sequence (SEQ ID NO:320). The Examiner states that one of ordinary skill would have been motivated to make such modification in order to "optimize the immune response induced by ... SEQ ID NO:888", and there would have been "a reasonable expectation of success ... because the determination of a workable range or optimal range is routinely practiced in the art."

Applicant respectfully disagrees. In making her obviousness determination, the Examiner first had to select a *single* nucleotide sequence from *over 1000 sequences* provided in Krieg et al.

SEQ ID NO:888 is not highlighted by Krieg et al. nor are data relating to that nucleotide sequence contained in the reference. To the contrary, Krieg et al. actually highlights other sequences as preferred and these differ from SEQ ID NO:888. The Examiner has provided no rationale for why one of ordinary skill would focus on SEQ ID NO:888 as a starting point.

The Examiner then applied the teaching of a modification of another sequence (SEQ ID NO:320) for another purpose to the selected sequence (SEQ ID NO:888). More specifically, the Examiner relied on the teaching in Krieg et al. that an exchange of an adenine located *between two CpG dinucleotides* for a thymidine (in SEQ ID NO: 320) resulted in greater activity. (See page 143, lines 16-31 of Krieg et al. in which a TCG ACG TT sequence located at the 5' end of SEQ ID NO: 320 was modified to TCG TCG TT.) Krieg et al. explicitly states, and the Examiner has apparently disregarded, that the modification to SEQ ID NO:320 was carried out in order to "determine the structure-function relationship of the CpG motifs" by replacing "the bases adjacent to the CpG dinucleotides while *maintaining the two CpG dinucleotides* within the sequence" (emphasis added). Krieg et al. emphasized the importance of having *two CpG dinucleotides* in this 5' modified stretch when it taught that "elimination of the first ... or the second ... CpG dinucleotide also partially reduced the activity". This is to be contrasted with the sequence in SEQ ID NO:888 which the Examiner desires to modify. This latter sequence, TTG ACG TT, contains only a single CpG dinucleotide and is located at the 3' end of SEQ ID NO: 888. There is no adenine located *between two CpG dinucleotides* because there is only one CpG dinucleotide in this sequence, and thus there should be no rationale for modifying SEQ ID NO: 888 as the Examiner indicates. The Examiner further relies on a teaching on page 154 of Krieg et al. to modify an internal (and relatively central) sequence in different nucleic acids (SEQ ID NOs: 343 and 344). This too is to be contrasted with the modification at the 3' end of SEQ ID NO: 888 which differs from SEQ ID NOs: 343 and 344.

The Examiner is using impermissible hindsight in making a prima facie case of obviousness. Nothing in Krieg et al. would have led the person of ordinary skill in the art to selectively choose SEQ ID NO: 888 over the more than 1000 sequences provided by the reference. Nothing in Krieg et al. would have led the person of ordinary skill in the art to selectively choose a particular sequence modification over the numerous sequence modifications provided by the reference. Only through knowledge of the instant application and the use of hindsight *might* one of ordinary skill in

the art have focused on and combined the particular teachings in Krieg et al. to arrive at the claimed nucleic acid sequence. Such hindsight however is impermissible.

Case law firmly supports that a reason must exist for one of ordinary skill in the art to choose a specific compound as a lead compound when presented with several other compounds. Takeda Chemical Industries, Ltd et al. v. Alphapharm Pty., Ltd et al. Case No. 06-1329 (Fed. Cir. June 28, 2007) (“Here, the court found nothing in the prior art to narrow the possibilities of a lead compound to compound b. In contrast, the court found that one of ordinary skill in the art would have chosen one of the many compounds disclosed in (the prior art), of which there were over ninety ...”); Eli Lilly and Company and Lilly Industries Limited v. Zenith Goldline Pharmaceuticals, Inc. et al. Case Nos. 05-1396, -1429, -1430 (Fed. Cir. Dec. 26, 2006) (“Furthermore, the trial court found that a person of ordinary skill in the art would not have chosen Compound ‘222 as the beginning compound because it contained a hydrogen atom instead of a halogen atom.”) Similarly, no motivation or teaching is provided in Krieg et al. to select SEQ ID NO: 888 as the starting sequence to modify. Case law also establishes that “a rejection cannot be predicated on the mere identification in [the reference] of individual components of claimed limitations”. In re Kotzab, 208 F.3d 1352, 54 USPQ2d 1308 (Fed. Cir. 2000) (“Rather, particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed.”); Takeda, Case No. 06-1329 (Fed. Cir. June 28, 2007) (“Even if that preliminary showing had been made (i.e., that compound b would have been selected as the lead compound), it failed to show that there existed a reason, based on what was known at the time of the invention, to perform the chemical modifications necessary to achieve the claimed compounds.”) Nothing in Krieg et al. leads the person of ordinary skill to selectively modify SEQ ID NO:888 based on the modification of SEQ ID NOs: 320, 343 and 344.

Applicant further stresses that the instant invention was based at least in part on the surprising discovery of a nucleotide sequence having activity that is the same as or greater than that of SEQ ID NO:246, one of the preferred sequences in Krieg et al. As described in the instant application, the claimed nucleotide sequence was identified after screening over 100 different sequences for such an activity profile. The activity profile of the claimed sequence and its

comparison to SEQ ID NO:246 are shown in the Examples. Clearly, in view of the extensive screening required, Krieg himself did not know and could not predict which sequence would have an activity profile approximating or exceeding that of SEQ ID NO:246. These facts strongly support the absence of the reasonable expectation of success necessary to make a prima facie case of obviousness, and/or the existence of unexpected results necessary to rebut a prima facie case even if made.

In view of the foregoing, the rejected claims are not obvious. Reconsideration and withdrawal of the rejection is respectfully requested.

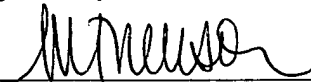
### CONCLUSION

Applicant respectfully requests reconsideration. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825, under Docket No. C1037.70043US00.

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Respectfully submitted,

By 

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